PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 56190

Title: Investigation of immune escape-associated mutations of hepatitis B virus (HBV) in patients harboring HBV drug-resistance mutations

Reviewer's code: 05288272

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2020-04-23

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-04-23 06:13

Reviewer performed review: 2020-04-27 08:56

Review time: 4 Days and 2 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

It is a good study that made a correlation among immune-escaped and drug-resistant mutations of HBV. You mentioned co.....without sA159V colocalization. Did you mean co-existence? If so, please correct throughout the manuscript

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Bixia Huang et al. investigated the link between the HBV immune escape-associated mutations (mainly the sA159V) and NA resistance mutations in a large cohort of chronic hepatitis B patients. This study is of clinical significance. But some issues remain to be addressed. 1. The role of the representative immune escape-associated mutation, sA159V, in the pathological process of chronic hepatitis B infection is suggested to be further clarified. For instance, the clinical outcome of the drug-resistant CHB patients with colocalization of sA159V should be compared with that of patients without the immune escape-associated mutation. 2. With the wide use of the new generation of potent oral NAs such as TAF, the incidence of drug resistance is decreasing rapidly, and its significance should be downgraded accordingly. The authors should mention it. 3. The authors are suggested to provide evidence to show the HBsAg quantitative assay (Roche Elecsys HBsAg) is not subject to the HBsAg mutations. Furthermore, in Table 3, "Analysis of clinical features in sA159V-positive and sA159V-negative patients", the unit of the HBsAg results is "COI". Actually, for the Roche Elecsys semi-quantitative HBsAg assay, results >5000 COI are very likely to reach the plateau, which means the results are beyond the upper semi-quantitative limit. They are not semi-quantitative results any longer. This might affect the statistical result between the two patient groups. 4. In Fig 2, the sequences from the patient A's samples are marked as "A1", "A2" and "A3". These taxon names are misleading because HBV Genotype A can be subtyped as A1, A2, and A3. Please rename them. 5. In the Results section, the sentence "HBsAg levels determined by an anti-HBs assay" is not correct; "M2–M5 were partly resistant to ETV sensitivity with 54.9%–64.7% inhibition. " Here the "sensitivity" should be deleted. 6. Ref 21, the guideline on prevention and treatment of chronic hepatitis B in China (2005) should be replaced with the version

of 2019.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 56190

Title: Investigation of immune escape-associated mutations of hepatitis B virus (HBV) in patients harboring HBV drug-resistance mutations

Reviewer's code: 03761093

Position: Peer Reviewer

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: China

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Reviewer chosen by: Dong-Mei Wang (Technical Editor)

Reviewer accepted review: 2020-07-08 02:31

Reviewer performed review: 2020-07-16 07:29

Review time: 8 Days and 4 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have improved the original MS according to my suggestions. No further comments in the re-review. I agree to accept the paper. Thank you.